REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Claims 1, 2, 5, 7, 8, 9 and 11 are amended herein. New claims 12-15 are added. Basis for the amendments and new claims may be found throughout the specification and claims as-filed, especially at page 6, lines 15-29 (dosages of loteprednol and azelastine); page 3, lines 13-15, page 4, lines 24-32 and Examples 1 and 3 on pages 9-11 (data for azelastine as an antihistamine, in combination with loteprednol).

Claims 3 and 6 are canceled without prejudice or disclaimer thereto. Applicants reserve the right to file at least one continuation or divisional application directed to any subject matter canceled by way of the present Amendment.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 5-9 and 11 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for a method of treating rhinoconjunctivitis, purportedly fails to provide enablement for treating all disorders of the lower and upper airway or treatment of all allergies.

In the interest of expediting prosecution, and without aquiesing in the rejection, Applicants have amended claims 5-9 and 11 herein to recite the treatment of allergic rhinitis and allergic conjunctivitis, as suggested by the Examiner on page 3 of the outstanding Office Action. Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 6-9 and 11 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Specifically, the Examiner argues that it is not clear in claims 6 and 9 whether the patient is required to have more than one disorder. As suggested by the Examiner, Applicants have amended the claims to recite the treatment of allergic conditions selected from the treatment of allergic rhinitis and allergic conjunctivitis. Thus, Applicants submit it is clear as to what disorders the patient in need of treatment is suffering from.

Claims 7 and 8 stand rejected as purportedly failing to further limit claim 5 from which they depend. Claims 7 and 8 are amended herein to depend from independent claim 9. Thus, this rejection is obviated.

Rejections Under 35 U.S.C. § 103

Claims 1-9 and 11 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Friedlaender. Friedlaender purportedly discloses that antihistamines are used as topically therapy for allergic conjunctivitis. Friedlaender also purportedly discloses that corticosteroid eyedrops, including loteprednol etabonate, are used to treat allergic conjunctivitis. The Office Action states that it would be obvious to the skilled artisan to combine loteprednol and an antihistamine.

Claims 1-9 and 11 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over European Patent No. 0 709 099 in view of WIPO Publication No. 97/01377. European Patent No. 0 709 099 purportedly discloses that loteprednol etabonate is used in the treatment of allergic rhinitis.

Applicants respectfully traverse.

In order to establish a case of *prima facie* obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See* M.P.E.P. §2142. Applicants respectfully submit that these criteria have not been met in the present Office Action.

Before turning to the cited references, Applicants note that the claims are amended herein to recite azelastine as the claimed antihistamine. Thus, the claims as amended herein recite a combination of loteprednol or ester thereof and azelastine.

Applicants respectfully submit that unexpected results are in fact present with respect to the claimed combination of loteprednol and azelastine.

It is a well established legal precedent that the presence of an unexpected, advantageous or superior result is evidence of nonobviousness. *See* M.P.E.P. § 716.02(a); *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963). It is also well established that "a greater than expected result" is evidence of nonobviousness. *See* M.P.E.P. § 716.02(a); *In re Corkill*, 711 F.2d 1496, 226 U.S.P.Q. 1005 (Fed. Cir. 1985).

As noted in Applicants' response of October 28, 2003, the present specification sets forth data showing an unexpected beneficial effect resulting from the combination of loteprednol and azelastine. Tables 1 and 2 of the specification (pages 5-6) show a highly significant overadditive effect in the combination of loteprednol and azelastine *in vitro* as well as *in vivo*. There is no motivation provided by Friedlander, or by the combination of European Patent No. 0 709 099 and WIPO

Publication No. 97/0137, to combine azelastine and loteprednol to achieve the unexpected result of the present invention. Applicants refer to the Examiner's comments in the Office Action on page 4, noting that the data provided in the specification is persuasive in this regard, as it applies to the combination of loteprednol and azelastine.

Turning to the cited references, Friedlander discloses the antihistamines for the treatment of allergic conjunctivitis. However, Friedlander fails to disclose or suggest the combination of the two substances as claimed in the instant invention or the unexpected benefits gained from the specific claimed combination.

European Patent No. 0 709 099, alone or in combination with the secondary reference, also fails to disclose the unexpected benefits of the claimed invention. European Patent No. 0 709 099 discloses an aqueous nasal suspensions of hardly soluble drugs with an example of loteprednol. This reference fails to provide any motivation for medical use, and fails to provide examples of a combination of loteprednol with antihistamines.

The secondary reference fails to remedy the deficiencies of the primary reference. WO 97/01377 discloses a nasal spray for the treatment of allergic rhinitis containing a combination of levocarbastine or azelastine together with a topical nasal steroid. However, the group of substances from which the reference states the steroid should be selected does not contain loteprednol, nor does the reference contain any data which would support the effectiveness or provide a motivation for the combination of the two substances.

Thus, in light of the above comments and in light of the amendments to the claims reciting the specific combination of loteprednol and azelastine, Applicants submit that the present claims are patentable over the cited references.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: July 28, 2004

By: _____
Deborah H. Yellin
Registration No. 45,904

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

VA 260878.1